

18/763,210

prelim andat = 1/26/04

Preliminary Amendment
1.53(b) Divisional of 10/009,332

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

Claims 1-11 (canceled).

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09/965,631

I 12. (original): An antibody against a metalloprotease having aggrecanase activity,
wherein said metalloprotease is selected from the group consisting of:

(a) a purified metalloprotease comprising an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(b) a purified metalloprotease comprising an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(c) a purified metalloprotease comprising an amino acid sequence selected from the group consisting of an amino acid sequence represented by amino acids 1-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1, and any one of said sequences wherein from 1 to 10 amino acid residues

are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity; and

(d) a purified metalloprotease comprising an amino acid sequence that has 90% or more sequence homology with the amino acid sequence set forth in SEQ ID NO:1, wherein said metalloprotease has aggrecanase activity.

II

13. (original): A method for screening a substance capable of inhibiting an aggrecanase activity of a metalloprotease, which comprises allowing the metalloprotease to contact a compound to be tested, wherein the metalloprotease is selected from the group consisting of:

(a) a purified metalloprotease comprising an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(b) a purified metalloprotease comprising an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(c) a purified metalloprotease comprising an amino acid sequence selected from the group consisting of an amino acid sequence represented by amino acids 1-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1, an amino acid sequence

represented by amino acids 213-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1, and any one of said sequences wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity; and

(d) a purified metalloprotease comprising an amino acid sequence that has 90% or more sequence homology with the amino acid sequence set forth in SEQ ID NO:1, wherein said metalloprotease has aggrecanase activity.

14. (original): A pharmaceutical composition for inhibiting degradation of *inhibitor*
proteoglycans, which comprises a substance capable of inhibiting a metalloprotease selected from the group consisting of:

(a) a purified metalloprotease comprising an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(b) a purified metalloprotease comprising an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 or an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1 wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity;

(c) a purified metalloprotease comprising an amino acid sequence selected from the group consisting of an amino acid sequence represented by amino acids 1-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 1-583 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-950 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-687 of SEQ ID NO:1, an amino acid sequence represented by amino acids 213-583 of SEQ ID NO:1, and any one of said sequences wherein from 1 to 10 amino acid residues are substituted, deleted and/or inserted, and wherein said metalloprotease has aggrecanase activity; and

(d) a purified metalloprotease comprising an amino acid sequence that has 90% or more sequence homology with the amino acid sequence set forth in SEQ ID NO:1, wherein said metalloprotease has aggrecanase activity.

IV 15. (original): A method of treating a joint disease, comprising administering to a patient in need of treatment a compound obtainable by the method of claim 13, thereby treating a joint disease.

V 16. (original): A polynucleotide represented by SEQ ID NO: 24, 25, 26, 27, 28, 29, 30 or 31, or a polynucleotide represented by SEQ ID NO: 24, 25, 26, 27, 28, 29, 30 or 31 and wherein from 1 to 10 nucleotide residues are substituted, deleted and/or inserted, wherein said polynucleotide has a joint disease aggrecanase promoter activity.

17. (original): A method for screening a substance capable of inhibiting aggrecanase
promoter activity, which comprises allowing a cell transformed with the polynucleotide
described in claim 16 to contact a compound to be tested.